



Wheat-dependent exercise-induced anaphylaxis with Tri-a-14-sensitization as part of a lipid transfer protein syndrome

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Received: 11 July 2018 / Accepted: 19 January 2019

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Keywords WDEIA · Lipid transfer protein syndrome · LTP · Tri a 14

Background

Wheat-dependent exercise-induced anaphylaxis (WDEIA) is the most common and best known form of food-dependent exercise-induced anaphylaxis (FDEIA) [1]. It is a summation anaphylaxis, in which the patient only shows an allergic reaction when eating wheat-containing food in combination with trigger factors, e.g. physical exercise, medical drugs (e.g. NSAIDs) or alcohol [1, 2]. The major allergen known for WDEIA is omega-5-gliadine (Tri a 19, a storage protein) [3]. Tri a 14 is a lipid transfer protein (LTP) in wheat. LTPs, which can be found in many different plants, are resistant to heat and digestion [4, 5].

Case representation

A 24-year-old man reported, after having consumed wheat-containing products (noodles, white bread) before physical exercise, to have reacted with an allergic reaction. He described symptoms like urticaria, angioedema, circulatory disturbance and a loss of consciousness. There was no history of other trigger factors, atopic disease or pollen sensitization. In an in vitro allergen-specific IgE test, we saw a CAP class rating ≥ 1 to Tri a 14, Pru p 3, Art v 3 and many other edibles (different types of flour, meal, also see Table 1), but not to Tri a 19, Pru p 1 and Pru p 4.

There were also negative results to gliadine IgG and gliadine IgA and only marginal levels of gluten/gliadin sIgE (Table 1). A skin prick test showed positive results to wheat flour, wheat noodles, spelt noodles, wheat popinos, white bread, cereals and other allergens. Negative results were found to egg, milk, soya, crab, shrimp, peanut, hazelnut, walnut, apple, orange, tomato and celery (Table 2).

The patient was hospitalized to perform a provocation test (results in Table 2). He showed allergic symptoms after eating four slices of white bread 30 min before physical exercise with moderate intensity (urticaria) and after drinking wheat beer before physical exercise (urticaria, angioedema, dyspnea, gastrointestinal symptoms). No reactions were seen after: wheat popinos; white bread; wheat noodles combined with physical exercise; wheat popinos combined with physical exercise; white wine combined with maize and/or physical exercise; peanut combined with white wine; and fruit salad combined with nuts.

Conclusion

WDEIA is the most common and best known form of FDEIA [1]. Approximately 80% of patients with WDEIA show positive test results to omega-5-gliadine (Tri a 19), but positive results to $\alpha/\beta/\gamma$ -gliadins have also been described [6].

Many patients with FDEIA show a sensitization to LTPs [2, 4]. LTPs can be found in many different plants [4]. Allergic reactions to LTPs often cause severe symptoms because they are neither fragmented nor degraded by digestion, and therefore highly reactive to IgE [4, 5]. Sensitizations to LTPs are often seen in Mediterranean regions [4, 5]. The cause of these findings is unknown. Genetic predisposition or food patterns are postulated [5].

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Table 1 Diagnostic findings

In vitro allergen-specific IgE test		
	kU/L	CAP
Pru p 1	0.00	0
Pru p 4	0.00	0
<i>Omega 5 gliadine (Tri a 19)</i>	0.02	0
Cat epithelia	0.03	0
Aspergillus fumigatus	0.03	0
Penicillium chrysogenum	0.03	0
Yeast	0.04	0
House dust mite	0.05	0
Dog epithelia	0.09	0
Gluten/Gliadin	0.53	1
Avocado	1.59	2
Kiwi	2.55	2
Maize	3.33	2
Wheat flour	8.32	3
Banana	9.40	3
Rye flour	9.57	3
Buckwheat flour	11.40	3
Sesame grist	11.70	3
Hazelnut	11.80	3
Barley flour	17.90	4
Mugwort	18.60	4
Peanut	19.10	4
Walnut	19.80	4
<i>Tri a 14</i>	21.40	4
Oat meal	22.20	4
Rice	24.90	4
<i>Art v 3</i>	40.80	4
Peach	41.90	4
<i>Pru p 3</i>	46.50	4
Maize meal	50.50	5
Sorghum	66.20	5
Other Ig tests		
	Measurement	Reference value
Total IgE (ECLIA)	335.6 IU/mL	<100 IU/mL
Gliadin-IgG (FIA)	<0.4 U/mL	<10 U/mL
Gliadin-IgA (FIA)	1.5 U/mL	<10 U/mL

CAP classes: 0: very low level of sIgE (<0.35 IU/mL); 1: low level of sIgE (0.35–0.69 IU/mL); 2: moderate level of sIgE (0.7–3.49 IU/mL); 3: high level of sIgE (3.5–17.49 IU/mL); 4: very high level of sIgE (17.50–49.9 IU/mL); 5: ultra high level of sIgE (50–99 IU/mL); 6: extremely high level of sIgE (>100 IU/mL), *Pru p* Prunus persica, *Tri a* Triticum aestivum, *Art v* Artemisia vulgaris, *ECLIA* electrochemiluminescence immunoassay, *FIA* fluorescence immunoassay, *Ig* immunoglobulin

Our patient shows clinical signs of WDEIA. Laboratory tests showed negative results to Tri a 19 but positive results to Tri a 14, suggesting a WDEIA as part of an LTP syndrome. Other sensitizations to LTP (Pru p 3, Art v 3) have been verified. sIgE to gluten/gliadin showed only a low level sensitization. Nevertheless it is described that there is no absolute correlation between sIgE values and severity. It is possible that

Table 2 Results of prick test and provocation test

Prick test		Provocation test	
Negative	Positive	No reaction	Allergic reaction
Egg	Wheat flour	Noodles wheat	<i>Wheat beer + E</i>
Milk	Noodles wheat	Wheat popinos	<i>White bread + E</i>
Soya	Spelt noodles	White bread	–
Crab	Wheat popinos	Noodles wheat + E	–
Shrimp	White bread	Wheat popinos + E	–
Peanut	Cereal	White wine + E	–
Hazelnut	Mango curry sauce	White wine + maize	–
Walnut	Ketchup	White wine + maize + E	–
Apple	Corn meal	Peanut + white wine	–
Orange	–	Fruit salad + nuts	–
Tomato	–	–	–
Celery	–	–	–
<i>E</i> physical exercise			

sensitization to other gliadins was not sufficiently detectable in our tests. However, our patient has had no allergic reactions when eating gliadin-containing foods without Tri a 14, which he obtains from a bakery declaring these ingredients. WDEIA as part of an LTP syndrome can be explained by the family background with ancestors from Hungary. Thanks to the provocation test, the patient can now better handle his allergy. The therapeutic suggestion was to avoid the combination of Tri a 14-containing food and trigger factors like physical exercise. He now keeps a Tri a 14-free diet and has not had allergic reactions since. He has got an emergency set and was informed about potential trigger factors.

Patients with WDEIA via LTPs were described in Italy [3], i.e. in the Mediterranean area, just as LTP sensitization in general. Nevertheless, this diagnosis should be taken in consideration also in the non-Mediterranean areas and patients should be questioned about their ancestors.

Conflict of interest M. Mickler, K. Drexler and S. Schreml declare that they have no competing interests.

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